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EXAMINER	
CARLSON, KAREN C	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,786	BOUWSTRA ET AL.	
	Examiner	Art Unit	
	Karen Cochrane Carlson, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *16-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's election without traverse of Group 1, Claims 1-11 and 15, in the reply filed on March 27, 2008 is acknowledged.

Upon search and examination of Group 1, the Examiner found art against Group 2 (Claims 12-14). Therefore, Claims 1-15 under under examination. Claims 16-19 have been withdrawn from further consideration by the Examiner because these claims are drawn to non-elected inventions.

Benefit of priority is to March 28, 2003.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: In Claim 8, the specification fails to provide antecdent basis for "less than 3%". See page 14 of the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In Claim 1 and 12, it is not clear if the gelatin having at least 350 amino acids must also have 0.4% RGD motifs because 1 RGD motif/350 amino acids is 0.29.

In Claim 3, it is not clear if the gelatin must have at least 250 amino acids, or 1.6% RGD motifs

In Claim 7, the limits of "less than about 150 kD", that is, is 160 kD "about 150 kD" and therefore the limitation is "less than 160 kD"? (or 125 kD, or 200 kD, etc).

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 8, 10, 11, 12, 13, and 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Chang et al. (USP 6,992,172, filed November 10, 2000).

Chang et al. teach gelatins comprising human collagen fragments (**Claim 10, 11**) consisting of SEQ ID NOs: 21 or NO: 29 (Col. 16, line 34+ and Example 1 at Col. 54). Additionally, it is art-recognized that the second proline of the GPP units in collagen is often hydroxylated.

SEQ ID NO: 21 comprises an RGD motif at amino acid 215 and 7 GPP units across this 251 amino acid sequence. Therefore, SEQ ID NO: 21 comprises 0.4% RGD motifs and potentially 2.8% hydroxyprolines (**Claim 8**). SEQ ID NO: 21 has a MW of 22.3 kD (Table 2 at col. 54).

SEQ ID NO: 29 comprises an RGD motif at position of this 100 amino acid sequence, or 1% RGD motifs (**Claim 2**). SEQ ID NO: 29 comprises 8 GPP (including 5 C-terminally added GPP units), and therefore has potentially comprises 8% hydroxyprolines. SEQ ID NO: 29 is the C-terminal half of SEQ ID NO: 28 (MW 17.9kD). Therefore, the Examiner would guess that SEQ ID NO: 29 would have a MW of about 9 kD (**Claim 13**).

Thus, Chang et al. teach an RGD enriched gelatin in which the percentage of RGD motifs is at least 0.4. These gelatins are fragments of native human collagen and comprise at least 30 amino acids that are native human collagens (**Claim 12**).

In Example 2, Chang et al. coated 96 well cell culture plates with the gelatin having SEQ ID NO: 21. Human foreskin fibroblasts and human umbilical vein endothelials cells were seeded onto the coated plates and the cells attached thereto (**Claims 1, 15**).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, and 5-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (USP 6,992,172, filed November 10, 2000).

Chang et al. teach gelatins comprising human collagen fragments (**Claims 10, 11**) consisting of SEQ ID NOs: 21, 22, 24, 25, 26, 28, 29, 30, and 33 (Col. 16, line 34+). Additionally, it is art-recognized that the second proline of the GPP units in collagen is often hydroxylated.

SEQ ID NO: 21 comprises an RGD motif at amino acid 215 and 7 GPP units across this 251 amino acid sequence. Therefore, SEQ ID NO: 21 comprises 0.4% RGD motifs and potentially 2.8% hydroxyprolines (**Claim 8**). SEQ ID NO: 21 has a MW of 22.3 kD (Table 2 at col. 54).

SEQ ID NO: 22 comprises an RGD at position 215 in the 500 amino acid sequence. Therefore, SEQ ID NO: 22 is greater than 350 amino acids and comprises one RGD motif per 350 amino acids. SEQ ID NO: 22 comprises 11 GPP units and therefore comprises potentially

comprises 2.2% hydroxyprolines (**Claim 8**). SEQ ID NO: 22 has a MW of 44.1 kD (Table 2 at col. 54; **Claim 5, 7**).

SEQ ID NO: 24 comprises an RGD motif at position 131 and has 3 GPP units in this 167 amino acid sequence. Therefore, SEQ ID NO: 24 comprises 0.6% RGD motifs (**Claim 2**) and potentially comprises 1.7% hydroxyprolines (**Claim 8**). SEQ ID NO: 24 has a MW of 14.9 kD (Table 2 at col. 55).

SEQ ID NO: 25 is a 416 amino acid sequence having an RGD motif at position 131. Therefore, SEQ ID NO: 25 is greater than 350 amino acids and comprises one RGD motif per 350 amino acids. SEQ ID NO: 25 comprises 11 GPP units, and therefore comprises potentially comprises 2.5% hydroxyprolines (**Claim 8**). SEQ ID NO: 25 has a MW of 36.8 kD (Table 2 at col. 55; **Claim 5, 7**).

SEQ ID NO: 26 is a 510 amino acid sequence (which would have a molecular weight of about 50 kD; **Claim 5**) having two RGD motifs, one at position 63 and the other at position 411. Therefore, SEQ ID NO: 26 comprises 0.4% RGD motifs and comprises at least one RGD motif per 350 amino acids. SEQ ID NO: 26 comprises 17 GPP units, having potentially comprises 3.3% hydroxyprolines (**Claim 8**).

SEQ ID NO: 28 comprises an RGD motif at position 101 in this 200 amino acid sequence, or 0.5% RGD motifs. SEQ ID NO: 28 comprises 10 GPP (including 5 C-terminally added GPP units), and therefore has potentially comprises 5% hydroxyprolines (**Claim 8**). SEQ ID NO: 28 has a calculated MW of 17.9 kD (Col. 56, line 7-8).

SEQ ID NO: 29 comprises an RGD motif at position of this 100 amino acid sequence, or 1% RGD motifs (**Claim 2**). SEQ ID NO: 29 comprises 8 GPP (including 5 C-terminally added GPP units), and therefore has potentially comprises 8% hydroxyprolines. SEQ ID NO: 29 is the C-terminal half of SEQ ID NO: 28. Therefore, the Examiner would guess that SEQ ID NO: 29 would have a MW of about 9 kD (**Claim 13**).

SEQ ID NO: 31 is a 251 amino acid sequence and comprises an RGD motif at position 131, or 0.4% RGD motifs. SEQ ID NO: 31 comprises 6 GPP units, and therefore has potentially comprises 2.3% hydroxyprolines (**Claim 8**). SEQ ID NO: 31 has a MW of 22.1 kD (Table 2 at col. 55).

SEQ ID NO: 33 is a 662 amino acid sequence and comprises an RGD motif at position 215 and 563 and therefore has an RGD motif for every 350 amino acids. SEQ ID NO: 33 comprises 24 GPP units (including 5 C-terminally added GPP units), and therefore has potentially comprises 3.6% hydroxyprolines (**Claim 8**). SEQ ID NO: 33 has a MW of 65 kD (Table 2 at col. 54; **Claim 5, 6, 7**).

Thus, Chang et al. teach an RGD enriched gelatins in which the percentage of RGD motifs is at least 0.4, and if the gelatin comprises at least 350 amino acids each stretch of amino acids contains at least one RGD motif. These gelatins are fragments of native human collagen and comprise at least 30 amino acids that are native human collagens (**Claim 12**).

Chang et al. do not expressly teach to coating cell culture plates with gelatins having SEQ ID NO: 22, 24, 25, 26, 28, 29, 30, and 33. However, throughout the specification, Chang et al. teach to use the gelatins as a graft coating, medical sponge, medical plug, and a microcarrier (Col. 6, lines 3-5; Col. 44, lines 44-46; Col. 45, para. 1) and to coat plates, flasks, microbeads, and other substrates with the gelatins for cell culture applications for cell attachment and growth (Col. 42, lines 58-61; Col. 51, lines 38-42). In Example 2, Chang et al. coated 96 well cell culture plates with the gelatin having SEQ ID NO: 21 (0.4% RGD motifs; potentially 2.8% hydroxyprolines; MW of 22.3 kD). Human foreskin fibroblasts and human umbilical vein endothelials cells were seeded onto the coated plates and the cells attached thereto.

It would have been obvious to a person having ordinary skill in the art to coat gelatins comprising SEQ ID NO: 22, 24, 25, 26, 28, 29, 30, and 33 onto a cell support such as in coating grafts (implant or transplant material), plates, flasks, microbeads (**Claim 14**), and other substrates with the gelatins for cell culture applications for cell attachment and growth (scaffold for tissue

engineering), or onto medical sponges (wound healing product) (**Claim 15**) because Chang et al. state that gelatins are useful as coatings for grafts, as sponges, and in cell culture applications. It would be predictable that these gelatins would be useful for these utilities because Chang et al. teach that non-recombinant gelatins are useful for these purposes and exemplify recombinant gelatins comprising SEQ ID NO: 21 as useful in cell culture applications for cell attachment and growth.

Claim 9 is included in this rejection because the gelatin of Claim 1 is met by the teachings of Chang et al. and therefore one would conclude that the gelatine would have a net positive charge at pH 7-7.5.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrari et al. (USP 6,140,072; issued October 31, 2000).

Ferrari et al. teach collagen like proteins (CLPs) having RGD motifs See Col. 36 to 41and Cols. 49-50 with regard to "Functional Polymers (CLP)".

SEQ ID NO: 66, 111, 112, 113, 114, and 115 are collagen like proteins comprising RGD motifs.

In SEQ ID NO: 66, five RGD motifs exist at amino acid positions 72, 132, 192, 252, and 312. Thus the CLP of SEQ ID NO: 66 comprises 1.41% RGD motifs in 355 amino acids. SEQ ID NO: 66 comprises 40 GPP units. Because the second proline of GPP units is often hydroxylated (Col. 36, line 23-24), SEQ ID NO: 66 may comprise 11.3% hydorxyprolines.

SEQ ID NO: 111 comprises 2 RGD motifs within 69 amino acids, or 2.9%. SEQ ID NO: 111comprises 7 GPP units, and therefore may comprise 10% hydorxyprolines.

SEQ ID NO: 112 comprises one RGD motifs within 69 amino acids, or 1.45%. SEQ ID NO: 112comprises 7 GPP units, and therefore may comprise 10% hydorxyprolines.

SEQ ID NO: 113 comprises one RGD motifs within 72 amino acids, or 1.4%. SEQ ID NO: 113 comprises 7 GPP units, and therefore may comprise 9.7% hydoxyprolines.

SEQ ID NO: 114 comprises 2 RGD motifs within 85 amino acids, or 2.4%. SEQ ID NO: 114comprises 8 GPP units, and therefore may comprise 9.4% hydoxyprolines.

SEQ ID NO: 115 comprises 2 RGD motifs within 83 amino acids, or 2.4%. SEQ ID NO: 115comprises 7 GPP units, and therefore may comprise 8.4% hydoxyprolines.

At page 4, para. 3 of the specification, the terms "collagen", "collagen-related", and "collagen-derived" are used interchangeably with "gelatine" and "gelatine-like". Indeed, the examples in the specification show gelatine as a single collagen like protein.

Ferrari et al do not specifically make cell supports comprising the gelatines taught therein, however, at Col. 36, Ferrari et al. teach that chemically hydrolyzed natural collagen can be denatured and renatured by heating and cooling to produce gelatin which is used in photographic and medical applications. At lines 44+, Ferrari et al. teach that the versatile formulation properties of collagen-like polymers makes them ideal as biomaterials used in implantable devices, used either as a coating on the surface of prostheses or as a structural component of the device itself, to promote tissue integration by providing improved blood and cellular interaction which is mediated in natural collagen by a specific 21 amino acid sequence SEQ ID NO: 50 (which comprises RGD). Thus, the CLPs taught in Ferrari et al. are considered to be gelatines.

It would have been obvious to a person having ordinary skill in the art to place the CLPs taught by Ferrari et al. that have at least 0.4% RGD motifs or at least 1.5% onto cell supports such as implantable medical devices because Ferrari et al. teach five CLPs having greater than 0.4% RGD motifs and state that the versatile formulation properties of collagen-like polymers makes them ideal as biomaterials used in implantable devices, used either as a coating on the surface

of prostheses or as a structural component of the device itself, to promote tissue integration by providing improved blood and cellular interaction (**Claim 1, 2**).

It is noted that in SEQ ID NO: 66, there are five RGD motifs (**Claim 4**) spanning amino acids 72-314, or at least 4 RGD motifs per 250 amino acids (**Claim 3**). SEQ ID NO: 66 consists of 355 amino acids in length, and therefore its molecular weight would be about 35 kD (**Claim 5, 7**).

Claim 6 is being included in this rejection because it is obvious to place amino acids on either side of a functional polypeptide such as the CLPs taught in Ferrari et al. **Claim 9** is included in this rejection because the gelatine of Claim 1 is met by the teachings of Ferrari et al. and therefore one would conclude that the gelatine would have a net positive charge at pH 7-7.5. **Claim 8** is included in this rejection because Ferrari et al. teach that the second proline in the GPP motif is *often* hydroxylated (Col. 36, line 23-24), but Ferrari et al. do not specifically teach that any of these prolines are hydroxylated or not. Thus, one cannot readily conclude that each of the second prolines of the GPP motifs found in the CLPs are hydroxylated.

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Cochrane Carlson, Ph.D. whose telephone number is 571-272-0946. The examiner can normally be reached on 7:00 AM - 4:00 PM, off alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1656

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen Cochrane Carlson, Ph.D./
Primary Examiner, Art Unit 1656